

What is claimed is:

1. An isolated protein having an apparent molecular weight of about 27 kD as measured by SDS polyacrylamide gel electrophoresis, and capable of binding to and inhibiting the activation of a cyclin E-Cdk2 complex.
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2. A recombinant nucleic acid molecule which encodes the protein of claim 1.
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3. The recombinant nucleic acid molecule of claim 2, wherein the nucleic acid molecule is a DNA molecule.
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4. The recombinant nucleic acid molecule of claim 3, wherein the DNA molecule is a cDNA molecule.
5. The recombinant nucleic acid molecule of claim 4, wherein the cDNA molecule is a mink cDNA molecule.
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6. The recombinant nucleic acid molecule of claim 5, wherein the mink cDNA molecule have substantially the same nucleotide sequence as described in Figures 13A and 13B.
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7. The recombinant nucleic acid molecule of claim 4, wherein the cDNA molecule is a mouse cDNA molecule.
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8. The recombinant nucleic acid molecule of claim 7, wherein the mouse cDNA molecule have substantially the same nucleotide sequence as described in Figures 14A and 14B.
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9. The recombinant nucleic acid molecule of claim 4,

wherein the cDNA molecule is a human cDNA molecule.

10. The recombinant nucleic acid molecule of claim 9,
wherein the human cDNA molecule have substantially
the same nucleotide sequence as described in Figures
15A and 15B.
11. The recombinant nucleic acid molecule of claim 2,
wherein the nucleic acid molecule is an RNA
molecule.
12. A vector comprising the recombinant nucleic acid
molecule of claim 4.
13. The vector of claim 12, wherein the vector is a
plasmid.
14. The plasmid of claim 13, designated pCMV5 p27kip1
(ATCC Accession No. _____).
15. The vector of claim 13, wherein the vector is a
virus.
16. A host vector system for the production of a protein
having an apparent molecular weight of about 27 kD
as measured by SDS polyacrylamide gel
electrophoresis, and capable of binding to and
inhibiting the activation of a cyclin E-Cdk2
complex, which comprises the vector of claim 13 in
a suitable host.
17. The host vector system of claim 16, wherein the
suitable host is a bacterial cell.
18. The host vector system of claim 16, wherein the
suitable host is an eucaryotic cell.

19. The host vector system of claim 18, wherein the eucaryotic cell is an insect cell.
20. A method for producing a protein having an apparent
5 molecular weight of about 27 kD as measured by SDS
polyacrylamide gel electrophoresis, and capable of
binding to and inhibiting the activation of a cyclin
E-Cdk2 complex, which comprises growing the host
vector system of claim 16 under conditions
10 permitting the production of the protein and
recovering the protein produced thereby.
- ✓ 21. A method of determining whether an agent is capable
of specifically inhibiting the ability of p27
15 protein to inhibit the activation of cyclin E-Cdk2
complex which comprises:
- (a) contacting suitable amounts of p27 protein,
cyclin E, Cdk2 and the agent under suitable
conditions;
 - 20 (b) subjecting the p27, cyclin E, Cdk2, and agent
so contacted to conditions which would permit
the formation of active cyclin E-Cdk2 complex
in the absence of p27 protein;
 - (c) quantitatively determining the amount of active
25 cyclin E-Cdk2 complex so formed; and
 - (d) comparing the amount of active cyclin E-Cdk2
complex so formed with the amount of active
cyclin E-Cdk2 complex formed in the absence of
30 the agent, a greater amount of active cyclin E-
Cdk2 complex formed in the presence of the
agent than in the absence of the agent
indicating that the agent is capable of
specifically inhibiting the ability of p27
protein to inhibit the activation of cyclin E-
35 Cdk2 complex.
- ✓ 22. A method of determining whether an agent is capable

of specifically enhancing the ability of p27 protein to inhibit the activation of cyclin E-Cdk2 complex which comprises:

- 5 (a) contacting suitable amounts of p27 protein, cyclin E, Cdk2 and the agent under suitable conditions;
- (b) 10 subjecting the p27, cyclin E, Cdk2, and agent so contacted to conditions which would permit the formation of active cyclin E-Cdk2 complex in the absence of p27 protein;
- (c) quantitatively determining the amount of active cyclin E-Cdk2 complex so formed; and
- 15 (d) comparing the amount of active cyclin E-Cdk2 complex so formed with the amount of active cyclin E-Cdk2 complex formed in the absence of the agent, a lesser amount of active cyclin E-Cdk2 complex formed in the presence of the agent than in the absence of the agent indicating that the agent is capable of 20 specifically enhancing the ability of p27 protein to inhibit the activation of cyclin E-Cdk2 complex.

23. A method of treating a subject having a 25 hyperproliferative disorder which comprises administering to the subject a therapeutically effective amount of an agent capable of specifically enhancing the ability of p27 protein to inhibit the activation of cyclin E-Cdk2 complex in the 30 hyperproliferative cells of the subject, so as to thereby treat the subject.

24. The method of claim 23, wherein the subject is a human.

35 25. The method of claim 23, wherein the hyperproliferative disorder is selected from the

group consisting of cancer and hyperplasia.

26. A method of treating a subject having a hypoprolifera-tive disorder which comprises administering to the subject a therapeutically effective amount of an agent capable of specifically inhibiting the ability of p27 protein to inhibit the activation of cyclin E-Cdk2 complex in the hypoproliferative cells of the subject, so as to thereby treat the subject.
27. The method of claim 26, wherein the subject is a human.
28. The method of claim 26, wherein the hypoproliferative disorder is an ulcer.
29. A method of diagnosing a hyperproliferative disorder in a subject which disorder is associated with the presence of a p27 protein mutation in the cells of the subject, which comprises determining the presence of a p27 protein mutation in the cells of the subject, said mutation being associated with a hyperproliferative disorder, so as to thereby diagnose a hyperproliferative disorder in the subject.
30. The method of claim 29, wherein the subject is a human.
31. The method of claim 29, wherein the hyperproliferative disorder is cancer.
32. A pharmaceutical composition which comprises an effective amount of a recombinant virus capable of infecting a suitable host cell, said recombinant virus comprising the nucleic acid molecule of claim

2, and a pharmaceutically acceptable carrier.

- 5 33. A method for treating a subject suffering from a hyperproliferative disorder associated with the presence of a p27 protein mutation in the cells of the subject, which comprises administering to the subject an amount of the pharmaceutical composition of claim 32 effective to treat the subject.
- 10 34. The method of claim 33, wherein the subject is a human.
- 15 35. The method of claim 33, wherein the hyperproliferative disorder is cancer.